Chemistry & Biology

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The core Alzheimer's peptide NAC forms amyloid fibrils which seed and are seeded by β-amyloid: is NAC a common trigger or target in neurodegenerative disease?
[Research Paper]
Hogyu Han, Paul H Weinreb, Peter T Lansbury, Jr
Chemistry & Biology 1995, **2**:163-169.

Abstract:

Backgound

NAC is a 35-amino-acid peptide which has been isolated from the insoluble core of Alzheimer's disease (AD) amyloid plaque. It is a fragment of α-synuclein (or NACP), a neuronal protein of unknown function. We noted a striking sequence similarity between NAC, the carboxyl terminus of the β-amyloid protein, and a region of the scrapie prion protein (PrP) which has been implicated in amyloid formation.

Results

NAC was prepared by chemical synthesis and was found to form amyloid fibrils via a nucleation-dependent polymerization mechanism. NAC amyloid fibrils effectively seed β_{1-40} amyloid formation. Amyloid fibrils comprising peptide models of the homologous β and PrP sequences were also found to seed amyloid formation by NAC.

Conclusion

The *in vitro* model studies presented here suggest that seeding of NAC amyloid formation by the β-amyloid protein, or seeding of amyloid fibrils of the β-amyloid protein by NAC, may occur *in vivo*. Accumulation of ordered NAC aggregates in the synapse may be responsible for the neurodegeneration observed in AD and the prion disorders. Alternatively, neurodegeneration may be caused by the loss of α-synuclein (NACP) function.